L Number	Hits	Search Text	DB	Time stamp
1	20	BoNT/A	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/07/10 15:35
2	13	BoNT/A and monoclonal	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/07/10 15:36
3	0	(BoNT/A and monoclonal) and 6b2-2	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/07/10 15:36
4	8	(BoNT/A and monoclonal) and botulism	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/07/10 15:36

2/9/6
DIALOG(R)File 155:MEDLINE(R)

10050455 99011483 PMID: 9795391
Identifying the principal protective antigenic determinants of type A botulinum neurotoxin.
Bavari S; Pless D D; Torres E R; Lebeda F J; Olson M A
Department of Cell Biology and Biochemistry, U.S. Army Medical Research Institute of Infectious Diseases, Frederick, MD 21702-5011, USA.
Vaccine (ENGLAND) Nov 1998, 16 (19) p1850-6, ISSN 0264-410X Journal Code: 8406899
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
The neurotoxins from Clostridium botulinum (BoNT serotypes A-G) exert their lethal effect by preventing the release of acetylcholine at the neuromuscular junction. As with tetanus toxin, immunization with a non-toxic fragment, the 50 kDa C-terminal portion of BoNT/A (Hc; residues 861-1296), protects mice against lethal challenges with the intact toxin. To locate the neutralizing epitopes, several protective monoclonal antibodies (mAbs) against BoNT/A-Hc were isolated and cloned. Specific binding of the mAbs to BoNT/A-Hc was demonstrated by surface plasmon resonance, with Kas in the range of 10(-10) to 10(-11) M. These antibodies recognized a genetically engineered polypeptide (1150-1289) that was previously shown to induce protective immunity. Prior to the determination of the X-ray crystal structure of the tetanus neurotoxin Hc fragment, molecular modelling studies indicated that it contained two highly solvent-exposed loops. Based on these predictions, two 25-mer Hc-peptides corresponding to these two regions were synthesized and were demonstrated to bind the neutralizing mAbs. Mice immunized with the Hc-peptides had high levels of antibodies that recognized BoNT/A-Hc. However, immunizations with only one of the Hc peptides protected when mice were challenged with BoNT/A. On the basis of these analyses, it should be possible to develop small peptides that could be useful in the design of future vaccines against these neurotoxins.
Tags: Animal; Female
Descriptors: *Bacterial Vaccines--immunology--IM; *Botulinum Toxin Type A --immunology--IM; *Epitopes--analysis--AN; Amino Acid Sequence; Antibodies, Bacterial--biosynthesis--BI; Antibodies, Monoclonal--immunology--IM; Antibodies, Monoclonal--metabolism--ME; Epitopes--immunology--IM; Mice; Mice, Inbred BALB C; Molecular Sequence Data; Neutralization Tests; Peptide Fragments--immunology--IM; Protein Conformation; Protein Structure, Secondary
CAS Registry No.: 0 (Antibodies, Bacterial); 0 (Antibodies, Monoclonal); 0 (Bacterial Vaccines); 0 (Botulinum Toxin Type A); 0 (Epitopes); 0 (Peptide Fragments)
Record Date Created: 19990106

8007235 94139688 PMID: 7508383

Antagonism of the intracellular action of botulinum neurotoxin type A with monoclonal antibodies that map to light-chain epitopes.

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European journal of biochemistry / FEBS (GERMANY) Jan 15 1994, 219 (1-2) p161-9, ISSN 0014-2956 Journal Code: 0107600

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

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mAbs were produced in mice against highly purified, renatured light chain (LC) of botulinum neurotoxin A (BoNT A) that was immobilised on nitrocellulose to avoid the undesirable use of toxoids. Subcutaneous implants of relatively high amounts (up to 10 micrograms each) of LC allowed its slow release into the systemic circulation and, thus, yielded much higher antibody titres against the underivatized antigen than had hitherto been obtained by conventional immunization. Seven stable hybridoma cell lines were established which secrete mAb of IgG1 and IgG2b subclasses reactive specifically with BoNT A and LC, in native and denatured states, without showing any cross-reactivity with types B, E, F or tetanus toxin. The pronounced reactivities of three mAbs towards refolded LC or intact toxin, observed in immunobinding and precipitation assays, relative to that seen in Western blots imply a preference for conformational epitopes. Though mAbs 4, 5 and 7 failed to neutralize the lethality of BoNT in vivo, administration intraneurally of mAb7 prevented the inhibition of transmitter release normally induced by subsequent extracellular administration of BoNT A. Notably, the latter mAb reacted with a synthetic peptide corresponding to amino acids 28-53 in the N-terminus of the LC, a highly conserved region in Clostridial neurotoxins reported to be essential for maintaining the tertiary structure of the chain. Most importantly, when mAbs 4 or 7 were microinjected inside ganglionic neurons of Aplysia, each reversed, though transiently, the blockade of acetylcholine release by the toxin; this novel finding is discussed in relation to the nature of the zinc-dependent protease activity of the toxin.

Tags: Animal; In Vitro; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.

Descriptors: *Antibodies, Monoclonal--pharmacology--PD; *Botulinum Toxins --antagonists and inhibitors--AI; *Botulinum Toxins--immunology--IM; *Neurons--drug effects--DE; *Neurotoxins--antagonists and inhibitors--AI; Amino Acid Sequence; Antibodies, Monoclonal--metabolism--ME; Aplysia; Enzyme-Linked Immunosorbent Assay; Epitopes--metabolism--ME; Mice; Mice, Inbred BALB C--immunology--IM; Multiple Myeloma; Neurons--physiology--PH; Neurotoxins--immunology--IM; Peptides--chemical synthesis--CS; Peptides --immunology--IM; Tumor Cells, Cultured

CAS Registry No.: 0 (Antibodies, Monoclonal); 0 (Botulinum Toxins); 0 (Epitopes); 0 (Neurotoxins); 0 (Peptides)

Record Date Created: 19940317

9/1
DIALOG(R)File 155:MEDLINE(R)

11278732 21318715 PMID: 11425742

Characterization of neutralizing antibodies and identification of neutralizing epitope mimics on the Clostridium botulinum neurotoxin type A.

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Applied and environmental microbiology (United States) Jul 2001, 67 (7) p3201-7, ISSN 0099-2240 Journal Code: 7605801

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Clostridium botulinum neurotoxin type A (BTx-A) is known to inhibit the release of acetylcholine at the neuromuscular junctions and synapses and to cause neuroparalysis and death. In this study, we have identified two monoclonal antibodies, BT57-1 and BT150-3, which protect ICR mice against lethal doses of BTx-A challenge. The neutralizing activities for BT57-1 and BT150-3 were 10(3) and 10(4) times the 50% lethal dose, respectively. Using immunoblotting analysis, BT57-1 was recognized as a light chain and BT150-3 was recognized as a heavy chain of BTx-A. Also, applying the phage display method, we investigated the antibodies' neutralizing B-cell epitopes. These immunopositive phage clones displayed consensus motifs, Asp-Pro-Leu for BT57-1 and Cys-X-Asp-Cys for BT150. The synthetic peptide P4M (KGTFDPLQEPRT) corresponded to the phage-displayed peptide selected by BT57-1 and was able to bind the antibodies specifically. This peptide was also shown by competitive inhibition assay to be able to inhibit phage clone binding to BT57-1. Aspartic acid (D(5)) in P4M was crucial to the binding of P4M to BT57-1, since its binding activity dramatically decreased when it was changed to lysine (K(5)). Finally, immunizing mice with the selected phage clones elicited a specific humoral response against BTx-A. These results suggest that phage-displayed random-peptide libraries are useful in identifying the neutralizing epitopes of monoclonal antibodies. In the future, the identification of the neutralizing epitopes of BTx-A may provide important information for the identification of the BTx-A receptor and the design of a BTx-A vaccine.

Tags: Animal; Support, Non-U.S. Gov't

Descriptors: *Antibodies, Monoclonal--immunology--IM; *Botulinum Toxin Type A--immunology--IM; *Clostridium botulinum--immunology--IM; *Epitopes, B-Lymphocyte; *Molecular Mimicry; Amino Acid Sequence; Antibodies, Bacterial--biosynthesis--BI; Antibodies, Bacterial--immunology--IM; Antibodies, Monoclonal--biosynthesis--BI; Botulinum Toxin Type A--chemistry --CH; Botulinum Toxin Type A--genetics--GE; Botulism--microbiology--MI; Botulism--prevention and control--PC; Enzyme-Linked Immunosorbent Assay;